

Are NMDA receptors involved in opiate-induced neural and behavioral plasticity? A review of preclinical studies

by

Trujillo KA.

Psychology Program,

California State University San Marcos,

92096-0001, USA.

keith@mailhost1.csusm.edu

***Psychopharmacology (Berl)* 2000 Aug; 151(2-3):121-41**

ABSTRACT

RATIONALE: Research over the past decade demonstrating that NMDA receptor antagonists have the ability to inhibit opiate tolerance, sensitization and physical dependence has led to the suggestion that NMDA receptors may have a critical role in opiate-induced neural and behavioral plasticity.

However, there have been suggestions that the effects of NMDA receptor antagonists on these phenomena result from non-specific behavioral or pharmacological effects, rather than from a specific inhibition of plasticity.

OBJECTIVES: To review the literature in order to explore whether the effects of NMDA receptor antagonists on opiate-induced changes in behavior are best accounted for by an inhibition of neural and behavioral plasticity, or if alternative explanations might better account for the results. **RESULTS:** The effects of NMDA receptor antagonists on the development of tolerance to opiate analgesia and the development of opiate physical dependence do not appear to be due to confounding behavioral effects produced by high doses of NMDA receptor antagonists, "side-effects" of a particular drug or drug class, blockade of associative learning processes, or state-dependency.

Results on tolerance and sensitization to the locomotor effects of morphine are more mixed and controversial; however, there is evidence suggesting that NMDA receptor antagonists may inhibit these phenomena in a similar manner. **CONCLUSIONS:** NMDA receptor antagonists appear to inhibit the neural plasticity underlying some forms of opiate tolerance, sensitization and physical dependence, suggesting that NMDA receptors are involved in the development of these drug-induced changes in behavior. Further research will help to determine the neural mechanisms responsible for these phenomena, and the therapeutic potential for drugs acting on the NMDA receptor complex in the treatment of pain and addiction.

Pain

Memantine

Zero tolerance?

NMDA antagonists

Pain and the NMDA receptor

NMDA antagonists for drug users

NMDA antagonists against morphine tolerance

NMDA antagonists, opioid receptors and tolerance